## REMARKS/ARGUMENTS

In response to the final Office Action of April 8, 2005, Applicants have amended the specification and claims, which, when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

In the Office Action of April 8, 2005, the Examiner has indicated that the amendment to the second paragraph on page 11 of the specification submitted previously is in improper format since "parameters" was inserted without underlining. By this amendment, Applicants have indicated that "parameters" is to be added to the paragraph by properly underlining the term. The amendment to the third complete paragraph on page 19 is also indicated as in improper format since "polyol" was inserted into the paragraph without underlining. As presently amended, polyol is indicated as having been inserted into the paragraph by underlining. The Examiner has also indicated that the amendment to claim 30 is in improper format due to "dioctylsuccinate" being changed to "dicotylsuccinate" without indicating the change with strikethrough and underlining as required by 37 C.F.R. §1.121(c)(2). By this amendment, "dioctylsuccinate" has been changed to "dicotylsuccinate" in claim 39 by indicating the change with strikethrough and underlining.

Claim 30 has been objected to since "dioctylsuccinate" is misspelled. By this amendment, the misspelling has been corrected.

Claim 1 has been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-12 of U.S. Patent No. 6,262,022. The rejection of claim 1 over U.S. Patent No. 6,262,022 will be resolved by an appropriate terminal disclaimer upon allowance of claims under consideration.

Claim 1 has been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-64 of U.S. Patent No.5,916,589. The position of the Examiner is that since claims 8 and 20 of the '589 patent recite cyclosporin-containing compositions which comprise a fatty acid triglyceride, and since claims 10 and 22 of the '589 patent recite a glycerol fatty acid partial ester (a monoglyceride such as glycerol monooleate), the claims of the '589 patent anticipate claim 1 of the present application. Applicants respectfully traverse the rejection for the following reasons. Claim 1 has been amended to recite: "[a] pharmaceutical composition for oral administration comprising: a) a cyclosporin as active ingredient in a carrier medium consisting essentially of b) a fatty acid triglyceride and c) a propylene glycol or sorbitol complete or partial ester, wherein the carrier medium is an oil based composition other than an oil-based aqueous emulsion and wherein the carrier medium is free of ethanol."

It is respectfully submitted that presently amended claim 1 is not merely an obvious variation of the invention claimed in the '589 patent. Use of propylene glycol or sorbitol complete or partial ester as a component in the carrier medium as recited in element c) of claim 1 is not suggested by the claims of the '589 patent. Nor is an oil based composition other than an oil-based aqueous emulsion suggested by the claims of the '589 patent. The claims of the '589 patent would simply not suggest to a skilled artisan, a pharmaceutical composition for oral administration comprising: a) a cyclosporin as active ingredient in a carrier medium consisting essentially of b) a fatty acid triglyceride and c) a propylene glycol or sorbitol complete or partial ester, wherein the carrier medium is an oil based composition other than an oil-based aqueous emulsion and wherein the carrier medium is free of ethanol, as presently recited in claim

1. Withdrawal of the rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting is therefore respectfully requested.

Claim 2 has been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-13 of U.S. Patent No. 5,652,212. The rejection of claim 2 over U.S. Patent No. 5,652,212 will be resolved by an appropriate terminal disclaimer upon the allowance of claims under consideration.

Claims 1, 27, and 29-37 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-22 of U.S. Patent No. 5,639,724. The rejection of claims 1, 27, and 29-37 over U.S. Patent No. 5,639,724 will be resolved by an appropriate terminal disclaimer upon the allowance of claims under consideration.

Claim 1 has been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,916,589. The '589 patent has been cited for teaching in Examples 1.6-1.8, cyclosporin-containing compositions comprising Miglyol 812 (which comprises fatty acid triglycerides) and glycerol monooleate (which is a glycerol fatty acid partial ester). As presently amended, claim 1 recites: "[a] pharmaceutical composition for oral administration comprising: a) a cyclosporin as active ingredient in a carrier medium consisting essentially of b) a fatty acid triglyceride and c) a propylene glycol or sorbitol complete or partial ester, wherein the carrier medium is an oil based composition other than an oil-based aqueous emulsion and wherein the carrier medium is free of ethanol." Since claim 1 no longer recites a glycerol fatty acid partial ester, claim 1 is distinguished from the teaching of U.S. Patent No. 5,916,589. Withdrawal of the rejection of claim 1 under 35 U.S.C.§ 102(e) is therefore respectfully requested.

Claim 1 has also been rejected under 35 U.S.C.§ 102(b) as allegedly anticipated by Cavanak (U.S. Patent No. 4,388,307). Cavanak has been cited for teaching

cyclosporin-containing compositions comprising saturated fatty acid triglycerides and mono- or di-glycerides of fatty acids (i.e., glycerol fatty acid partial esters). Since presently amended claim 1 no longer recites a glycerol fatty acid partial ester, claim 1 is distinguished from the teaching of Cavanak. Applicants therefore respectfully request withdrawal of the rejection of claim 1 under 35 U.S.C. § 102(b).

Claims 1, 27, 29, 30, and 32-37 have been rejected under 35 U.S.C.§ 102(b) as allegedly anticipated by the Belgian Patent '724 in view of Applicants' admission of the prior art at page 9, lines 26-30; page 15, lines 17-32; and page 19, lines 16-18 and 21-22 of the specification. The Belgian '724 patent is cited for teaching cyclosporin compositions comprising Dihydrocyclosporin D and a carrier medium comprising ethanol, MAINSE 7 and optionally CREMOPHOR7 RH 40 or IMWITOR7 742 or LABRAFIL 7 2125. The Examiner has indicated that MAISNE 7 is the tradename of a trans-esterification product of corn oil with glycerol, comprising triglycerides, diglycerides, monoglycerides and free glycerol in the ratios claimed by Applicants. The Examiner has indicated that Example 2 of the Belgian '724 patent is substantially free of ethanol.

As presently amended, claim 1 recites: "[a] pharmaceutical composition for oral administration comprising: a) a cyclosporin as active ingredient in a carrier medium consisting essentially of b) a fatty acid triglyceride and c) a propylene glycol or sorbitol complete or partial ester, wherein the carrier medium is an oil based composition other than an oil-based aqueous emulsion and wherein the carrier medium is free of ethanol."

Support for the subject matter of claim 1 may be found throughout the specification, e.g., page 10, lines 27-38, which discloses: "[i]n a specific aspect the present invention provides for oil-based pharmaceutical compositions, in particular, oil-based pharmaceutical compositions other than aqueous emulsions, which are free or

substantially free of ethanol. Examples 1-3 and 5-7 further support claim 1 as amended as the formulations exemplified therein are free of ethanol. (In contrast, Example 4 of the present application discloses a formulation where ethanol is present in a quantity of 2-5%, a quantity the Examiner considers "substantially free of ethanol." *See* Office Action, page 3, final sentence.) Claim 1 in reciting "wherein the carrier medium is free of ethanol" is distinguished from the teaching of the Belgian Patent '724 which teaches formulations having ethanol, e.g., Example I, where ethanol is present in a quantity of 10-12% and Example II, where ethanol is present in a quantity of 2-5%. Since claim 1 presently recites "and wherein the carrier medium is free of ethanol", the claim is distinguished from the teaching of the Belgian '724 patent. Withdrawal of the rejection of claims 1, 27, 29, 30, and 32-37 under 35 U.S.C.§ 102(b) is therefore respectfully requested.

Claim 31 has been rejected under 35 U.S.C. §103(a) as allegedly obvious over the Belgian Patent '724 in view of Applicants' admission of the prior art at page 9, lines 26-30, page 15, lines 17-32; and page 19, lines 16-18 and 21-22, of the specification. The Examiner has directed Applicants to Example I of the Belgium Patent '724, where the ratio of Dihydrocyclosporin D to "CREMOPHOR7 RH 40" is not 1:at least 1." However, according to the Examiner, it would have been obvious to one of ordinary skill to determine all operable and optimum proportions of Dihydrocyclosporin D and "CREMOPHOR7 RH 40" for use in the invention of the Belgian Patent '724 since its disclosure is not limited to any particular proportions of components in its pharmaceutical compositions and because it is routine in the art to determine all operable and optimal proportions of components in pharmaceutical compositions.

Applicants traverse the rejection of claim 31 under 35 U.S.C.§ 103(a) for the following reasons. Claim 31 eventuates from claim 1 and claim 1 presently recites

"wherein the carrier medium is an oil based composition other than an oil-based aqueous emulsion and wherein the carrier medium is free of ethanol." Both working examples in the Belgian Patent '724 disclose formulations having ethanol. There is no suggestion in the Belgian Patent '724 for a carrier medium free of ethanol regardless of the fact that the Belgian Patent '724 may or may not be limited to any particular proportions of components in its pharmaceutical compositions. Withdrawal of the rejection of claim 31 under 35 U.S.C.§ 103(a) is therefore respectfully requested.

Claim 1 has been rejected under 35 U.S.C.§ 102(b) as allegedly anticipated by Chemical Abstract 92:64765k. Chemical Abstract 92:64765k has been cited for teaching a pharmaceutical composition comprising Cyclosporin A, an ester of a triglyceride with a polyalkylene glycol, e.g. "LABRAFIL M 1944", a fatty acid triglyceride, and a mono- or di-glyceride. The abstract teaches compounds having a pharmacodynamic active monocyclic peptide and a support consisting of a nonionizing ester of a triglyceride with a polyalkylene glycol, fatty acid triglyceride and a mono-or diglyceride were prepared. Specifically, the compound was prepared by mixing 200 mg of cyclosporin A with 1 mL of a mixture of Labrafil M 1944 and ethanol (40:15) at 25° C, followed by addition of 0.4ml of olive oil or corn oil and filtration.

It is respectfully submitted that the pharmaceutical composition of Abstract 92:64765k comprises ethanol since it is prepared by mixing Labrafil M 1944 and ethanol in a ratio of 40:15. Presently amended claim 1 recites in relevant part: "wherein the carrier medium is free of ethanol." Claim 1 is therefore distinguished from the teaching of Abstract 92:64765k, and withdrawal of the rejection of claim 1 under 35 U.S.C.§102(b) is therefore warranted.

In view of the foregoing remarks, it is respectfully submitted that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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